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William Stokes, DVM, DACLAM
Director
NICEATM
National Toxicology Program
PO Box 12233, MD EC-17
Research Triangle Park, NC 27709

RE: Public Comment on *In Vitro* Test Methods for Detecting Ocular Corrosives and Severe Irritants

Dear Dr. Stokes:

This public comment is delivered in response to Federal Register Notice Volume 69, Number 212, Pages 64081-64082. It addresses the Background Review Document (BRD), "Current Status of In Vitro Test Methods for Identifying Ocular Corrosives and Severe Irritants: The Bovine Opacity and Permeability (BCOP) Test Method", November 1, 2004.

As a contract research laboratory, MB Research has performed over 5,500 BCOP assays since 1993. Therefore, I feel it necessary to comment on the Committee's recommendation for additional validation studies as well as the assays' lack of usefulness in predicting low-level irritancy. Most of the 5,500 BCOP assays were performed in combination with either the Chorioallantoic Membrane Vascular Assay (CAMVA) or the EpiOcular ™ tissue equivalent assay. Generally, these combination of assays have been performed for clients who use them in their decision-making processes for the determination of ocular irritation potential of cosmetics and personal care products. Routinely, the results of these assay fall in the non-irritating to slightly-irritating ranges.

Annually, over 200 Draize eye irritation assays are performed for regulatory submission at MB Research and since 1972, we have assayed over 8,800 materials in the Draize test. I and my technicians look forward to the time when the rabbit study will be replaced, but realize that the replacements should have similar attributes as the Draize test– inexpensive, rapid, and capable of making analagous comparison of human exposure.

Inexpensive: The present cost for a 3 rabbit eye irritation study using OPPTS guidelines is $765 for a 3-day study and up to $1,715 for a 21-day study. The cost for the BCOP/CAMVA assay is $1,270. The BCOP/EpiOcular combination is $1,885. Both are in the same range as the Draize.

Rapid: Since either of the combination assays can be started within one to two weeks, and are one or two day assays, they are actually quicker then the Draize.

Analagous Comparison: The results of the combination assays are analagous to Draize results given a familiarity with the idiosyncrasies of each assay.

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I have attached copies of MB Research validation studies for the BCOP. In addition, we have also performed numerous validation assays for clients to prove the effectiveness of the BCOP, BCOP/CAMVA, and BCOP/EpiOcular for routine analysis of specific type of products. Unfortunately, the majority of the latter information is not available due to confidentiality agreements with the sponsors.

While the Draize test can be considered the gold standard against which all alternative are assessed, given the problems of interpretation and interlaboratory variability it is only a 10-karat gold standard. We need to develop a 24-karat alternative. I believe that two or three alternative assays with appropriate conservative endpoints will provide rapid answers to the questions for eye irritancy without the use of animals. I suggest rather, than multi-group validations, that the Institute for In-Vitro Science be given a mandate to develop and validate two or three assays with criteria that will meet regulatory acceptance.

We at MB Research support your efforts to find alternatives to the Draize test and look forward to the elimination of rabbits in ocular irritancy testing.

Sincerely,

Daniel R. Cerven, MS
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